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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/355,214	07/23/99	CHAN A	A-64383-2

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EXAMINER	
ZITOMER,S	
ART UNIT	**PAPER NUMBER**
1655	7

DATE MAILED: 12/08/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/355,214	Applicant(s) CHAN et al.
	Examiner Stephanie Zitomer	Group Art Unit 1655

☒ Responsive to communication(s) filed on *Oct 6, 2000* .

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). *Extensions of time may be obtained under the provisions of* 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *23-34* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *23-34* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Application status

1. Receipt of the amendment filed October 6, 2000 is acknowledged.

2. Rejections not iterated herein from the previous Office action, paper no. 4, mailed March 29, 2000, have been withdrawn as being obviated by cancellation of claims 1-22. Rejections applied to new claims 23-34 are set forth below. All of applicant's arguments have been fully considered.

Defective oath

3. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See M.P.E.P. §§ 602.01 and 602.02. The oath or declaration is defective because the parent application, 08/819,013, and the grandparent application, 08/788,322 are incorrectly listed as abandoned and pending, respectively. The former has been patented and the latter has been abandoned.

Improper incorporation by reference

4. The attempt to incorporate essential subject matter into this application by reference to publications by Maniatis et al. and Ausubel et al. (page 8) is improper. The subject matter is "high stringency conditions" and it is essential because it is a limitation in claims 25 and 28. The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejections under 35 U.S.C. 101 and 112, first paragraph: Lack of utility and enablement

5. Claims 23-34 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. The nature of the claimed invention is such that the activity of the BLNK protein has not been defined and is largely speculative based on the ability to bind other B cell proteins. The specification teaches that the claimed BLNK protein interacts with various B cell proteins including Grb2, PLCγ, nck, Vav and phospholipase C following BCR activation (page 19). It is stated further that a function of BLNK "is to modulate the ability of the B cell receptor to regulate calcium levels in the cell" (page 19, lines 7-9). However, modulation of BCR regulation of calcium levels is not shown to be a factor in any disease or condition treatable with a BLNK protein nor has any other disease or condition been shown to be associated with the activity of a BLNK protein. Therefore, the asserted utility is a general utility, not a specific utility for treating a specific disease or condition. Furthermore, the asserted utility of BLNK proteins as specific B-cell markers (page 19, lines 19-23) is also a general utility because the finding that they are more highly expressed in B-cells relative to other cell types is not novel in that other proteins can be used as B-cell specific markers in the same way. Note that because the claimed invention is not supported by a specific asserted utility credibility cannot be assessed.

6. Claims 23-34 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Response to applicant's arguments traversing lack of utility and enablement rejections

7. Applicant's arguments filed October 6, 2000 have been fully considered but they are not persuasive. They have been considered as they apply to the rejections of the new claims. The arguments are stated to be based on the "new guidelines set forth by the Patent Office for determining utility" but do not cite the publication venue. This response relies on the "Guidelines for Examination of Applications for Compliance With the Utility Requirement" published in the Federal Register on December 21, 1999 (Vol. 64, No. 244). It is pointed out that the first consideration of utility is that it must be a specific and

substantial utility, whether asserted by applicant or well established in the prior art (page 71441, II. B. 2. (a) and (b)). The examiner is admonished not to make a rejection for lack of utility if a utility asserted in the specification is specific and substantial. The argument extrapolates information provided in the specification to arrive at a "logical" conclusion of utility. For example, it is opined that "if a BLNK protein affects signaling mechanisms that lead to B-cell activation and alterations in B-cell activation are associated with particular dysfunctions, then said dysfunctions will be beneficially treated by administration pf a pharmaceutical compound comprising a BLNK protein". This "logic" is flawed because the primary operatives, specific and substantial, are missing. Tellingly, the summary of BLNK protein activities (arguments at page 8) is rife with indefinite terms such as "will lead to", "associates with" and "is implicated". The "association" of B-cell hypoactivation and immunodeficiency disorders, the "association" of B-cell hyperactivation with autoimmune disorders and the "association" of alterations in B-cell activation with "certain B-cell tumors" are cited as concepts known in the prior art. However, the arguments fail to make a nexus between these concepts and the claimed invention proteins. The cited papers published after the filing date of the application demonstrate that further research on BLNK proteins has not established a specific and substantial utility for the claimed invention proteins. Therefore, applicant's arguments regarding utility are not persuasive.

Rejection under 35 U.S.C. 112, first paragraph: Lack of written description

8. Claims 23-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to a very large genus of recombinant polypeptide species comprising the protein of SEQ ID NO:1, polypeptides comprising an amino acid sequence at least 95% identical to SEQ ID NO:!, species of nucleic acids encoding the protein or hybridizing to SEQ ID NO:2 and species of antibodies to the protein. In addition to enablement the first paragraph of 112 requires a "written description". As set forth by the Court in *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, the written description must convey to one of skill in the art "with reasonable clarity" that as of the filing date applicant was in possession of the claimed invention. The specification

describes the protein, BLNK1, and its splice variant, BLNK2, and discloses the amino acid sequence of BLNK1 (SEQ ID NO:1) as well as the nucleotide sequence encoding it (SEQ ID NO:2). However, the specification is silent regarding the sequences of other BLNK protein and nucleic acid species to which the claims are drawn. The specification does not describe any of the large number of nucleic acids and peptide species encompassed by the claims which encode a recombinant polypeptide comprising SEQ ID NO:1, hybridize to the SEQ ID NO:2 nucleotide sequence or which have at least 95 percent identity to these nucleotide and amino acid sequences as well as the claimed methods, compositions and antibodies involving the nucleic acid and polypeptide or coding or amino acid sequence species encompassed by the claims. The claims encompass a very large number of nucleic acids and proteins only one of which in each category is disclosed. The specification states at page 5 that nucleic acids and proteins having a given percent homology may be "determined using standard techniques known in the art, such as the Best Fit program... or the BLASTX program" and that "alignment may include the introduction of gaps in the sequences to be aligned". This loose description of how the claimed sequences may be found does not provide sufficient teaching or guidance to enable one skilled in the art to determine the specific sequences that are within the scope of the claims. No specific algorithm used for alignment nor the Gap or Gap Extension Penalties is disclosed. At page 15 the specification states that the invention includes "amino acid sequence variants" of three types: "substitutional, insertional or deletional" and may be "fragments" of BLNK proteins (lines 20-29). Pages 16-17 discuss the kinds of amino acid substitutions that may be brought about by mutation but no teaching or guidance is provided as to which residues of the proteins may be substituted or deleted or which amino acids are to be inserted at which positions. For example, in a 456 amino acid sequence comprising 95% identity to SEQ ID NO:1, 23 residues may be removed *en bloc* from either terminus or from any internal position or 23 residues may be changed at indeterminate positions along the length of the protein. Similarly, in a 1086 nucleotide sequence, 90 nucleotides may be changed whereas no guidance is provided for determining the nucleotide positions to be altered. The court stated in *Amgen, Inc.* v. *Chugai Pharmaceutical Co. Ltd*, 18 USPQ2d, 1016,

> Conception of chemical compound requires that

> inventor be able to define compound so as to distinguish it from other materials, and to describe how to obtain it, rather than simply defining it solely by its principal biological property; thus, when inventor of gene, which is a chemical compound albeit a complex one, is unable to envision detailed constitution of gene so as to distinguish it from other materials, as well as method for obtaining it, conception is not achieved until reduction to practice has occurred, and until after gene has been isolated.

Further, the specification states at page 15 that "rabbit polyclonal" and "mouse monoclonal" antibodies to BLNK fusion proteins were made. However, these antibodies are not described: not as to their type nor the epitopes to which they bind nor the procedures by which they were made. Absent description of a reasonable number of nucleic acid, polypeptide and antibody species the specification cannot convey to one of skill in the art that applicant possessed the large genus of claimed nucleotide and amino acid sequences and antibodies as of the date the application was filed.

Rejection under 35 U.S.C. 112, second paragraph: Indefiniteness

9. Claims 1-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claim 23 is confusing at "polypeptide comprising the protein" because neither term has a standardized meaning as to size and structure and it is unclear in the claim how the one relates to the other. It is suggested to use a single term, "polypeptide" or "protein" to avoid ambiguity.

(b) Claims 25 and 28 are indefinite at "high stringency conditions" because the phrase has no standardized meaning in the art and such not defined in the specification. While one of skill in the art may determine "high stringency conditions" for a specific application as suggested at page 8, absent definition of the "conditions" one of skill in the art would not be apprised of the scope of the claimed invention. It is suggested to recite specific hybridization conditions according to the specification, if any.

(c) Claims 27 and 31-34 lack proper antecedent basis in depending from canceled claims and from claims which do not recite "polypeptide". It is suggested to change the claim dependency or to incorporate the subject matter relied on in the canceled claims into the present claims.

Conclusion

11. No claim is allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephanie Zitomer whose telephone number is (703) 308-3985. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152. The official fax phone number for this Group is (703) 308-4242. The unofficial fax number is (703) 308-8724.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

S. Zitomer

Stephanie Zitomer, Ph.D.
December 7, 2000